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Steroidal Sapogenins. XXXVIII.[1] 5-Pregnene-3β,17α-diol-12,20-dione 3-Acetate

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In a previous publication[2] we described the preparation and properties of a new 12-keto sapogenin, gentrogenin. In continuation of previously described researches on 12-keto compounds of the C_{21} series[2] we have used gentrogenin as a source of C_{21} compounds containing both the 12-keto group and the 5,6-olefinic bond. It will be recalled that the sapogenin degradation product 5,16-pregnadien-3β-ol-12,20-dione acetate prepared by Marker[3] was reported to melt from 226 to 228°, while our product, I, from gentrogenin melted from 173 to 175°.[2]

In this present note we wish to describe the conversion of our 5,16-pregnadien-3β-ol-12,20-dione acetate, I, of melting point 173–175° to the 16α,17α-epoxide, II, and subsequently to the derived bromohydrin, III, and 17α-hydroxy desbromo compounds, IV. This route for introduction of the 17α-hydroxyl group was first used by Julian, *et al.*[4] Parallels to the present reactions have been described in the hecogenin series[5] and diosgenin series[4]; however, in the present case the analogy could not be followed to the point of introduction of the 21-acetoxy group. We were not able to prepare 3β,21-diacetoxy-5-pregnen-17α-ol-12,20-dione from IV by treatment in sequence with bromine, potassium iodide, and sodium acetate.[6]

EXPERIMENTAL

16α,17α-Epoxy-5-pregnen-3β-ol-12,20-dione Acetate, II 5,16-Pregnadien-3β-ol-12,20-dione acetate, 0.63 g., was dissolved in 80 ml. of methanol. To the solution cooled in an ice bath was added 5 ml. of 30% hydrogen peroxide followed by 2.3 ml. of 4*N* sodium hydroxide. After storing overnight at 10°, 80 ml. of water and 2.3 ml. of 4*N* hydrochloric acid were added. On concentration of the solution *in vacuo* to 40 ml., a crop of crystalline plates separated and was collected by filtration. A small additional amount of product was isolated by extracting the filtrate with methylene chloride. Acetylation of the product with 60 ml. of 1:1 acetic anhydride-pyridine overnight at room temperature, dilution with water, extraction with ether, washing the organic layer with dilute hydrochloric acid and dilute sodium bicarbonate, drying with sodium sulfate, and concentration to 50 ml. gave a crystalline precipitate of 512 mg. of hexagonal, broad blades, m.p. 235.8–236.3°. Concentration to 7 ml. gave an additional crop of 88 mg., total yield 89%. The analytical sample, recrystallized from ether, showed transition to long spicules, m.p. 238.0–238.2°, $[\alpha]_D^{25}$ +29.4° ($CHCl_3$).

Anal. Calcd. for $C_{23}H_{30}O_5$: C, 71.48; H, 7.82. Found: C, 71.44; H, 7.99.

16β-Bromo-5-pregnene-3β,17α-diol-12,20-dione 3-Acetate, III. A solution of 500 mg. of epoxide in 15 ml. of glacial acetic acid was cooled to 15° and treated with 5 ml. of a solution of 2 ml. of 48% hydrobromic acid dissolved in 12 ml. of acetic acid. After standing 16 hr. at room temperature, the solvents were evaporated at 35° under water-aspiration. The slushy residue was diluted with ether, and the organic layer was washed with water, 2% sodium bicarbonate, and saturated brine, and after drying with sodium sulfate, was concentrated to 30 ml. on the steam bath and allowed to evaporate slowly, depositing 510 mg. of large hexagonal prisms, m.p. 214–217°, yield 86%. Recrystallization was effected by dissolution in a minimal volume of methylene chloride, dilution with ether, and boiling to remove the methylene chloride azeotropically. Repeated crystallization by this procedure gave dense polyhedra undergoing transition over 190° on the Kofler block to hexagonal plates with characteristic degenerate trapezoidal forms having a double melting point within the narrow range 219.2 to 220.5°, $[\alpha]_D^{25}$ −35°. The infrared carbonyl spectrum strongly resembled that of the hecogenin analogue shown in figure 1-A in reference 5 with strong bands at 1734, 1720, and 1695 cm.$^{-1}$.

Anal. Calcd. for $C_{23}H_{31}BrO_5$: C, 59.10; H, 6.69; Br, 17.10. Found: C, 59.28; H, 6.92; Br, 17.57.

5-Pregnene-3β,17α-diol-12,20-dione 3-Acetate, IV. The epoxide, 4.8 g. in 144 ml. of glacial acetic acid, and 48 ml. of hydrobromic acid in 200 ml. of acetic acid were mixed and reacted as described above. The solvents were evaporated under reduced pressure (water aspirator). The semisolid residue in acetone acidified with 3 ml. of acetic acid

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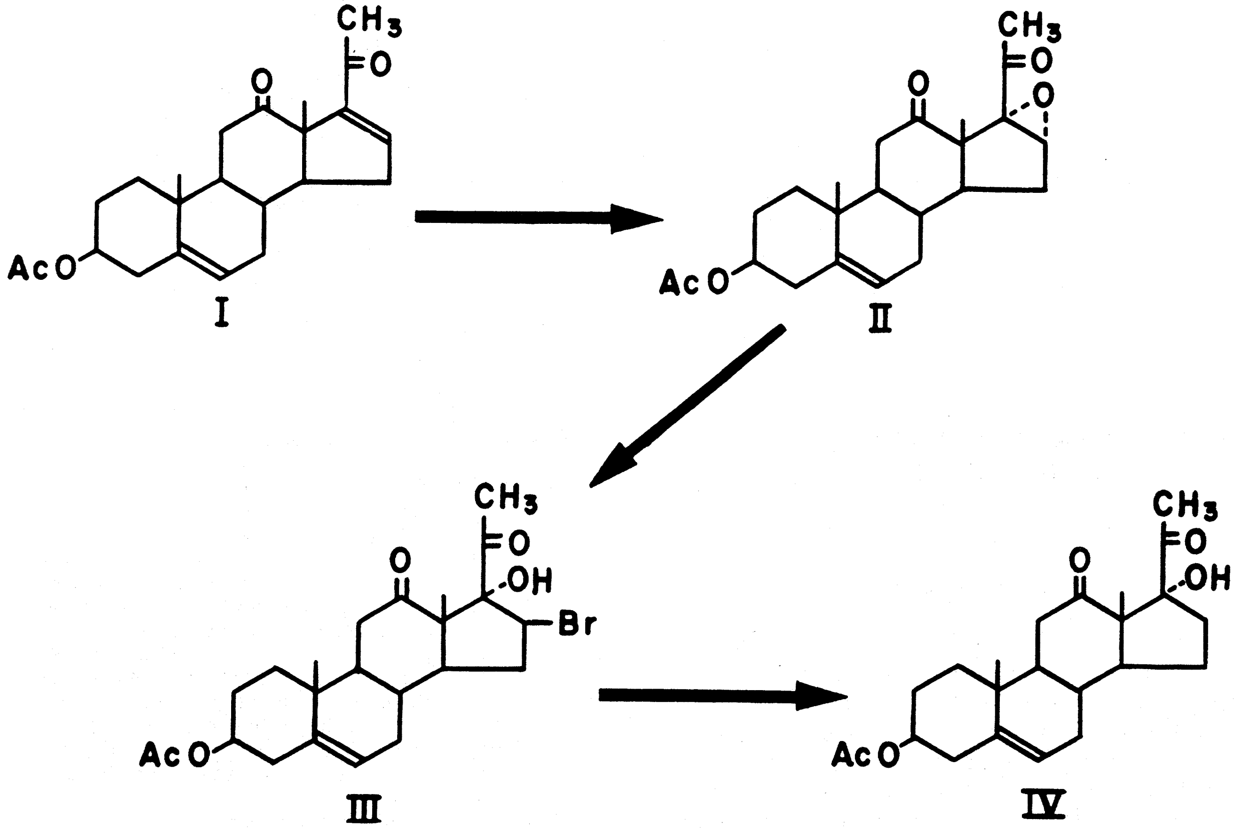

was refluxed 4 hr. with 48 g. of a Raney nickel catalyst. The catalyst was prepared from the alloy using Adkins' directions[7] modified by the acetone inactivation method of Barkley, *et al.*[8] The catalyst was filtered off and the solvents were evaporated. Trituration of the residue with ether gave 4 g. of dense granular polyhedra melting at about 170°, yield 83%. Recrystallization from cyclohexane (dense, granular crystal forms) and from methanol gave needles m.p. 181.0–182.2° with incomplete transition to plates, $[\alpha]_D^{25}$ −23.3°. The carbonyl infrared spectrum strongly resembled that of the hecogenin analog, Figure 1-B in reference 5, showing strong bands at 1735, 1706, and 1694 cm.$^{-1}$.

Anal. Calcd. for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 71.06; H, 8.31. An experiment using highly purified, isolated bromohydrin and a portion of the same Raney nickel catalyst used in the above experiment gave reversion of the bromohydrin to the epoxide.

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